PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

C1

To:
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RECOMMANDE

Date of mailing *(day/month/year)*	03/10/2001
Applicant's or agent's file reference: 21402-138	**PAYMENT DUE** within 45 ~~months~~/days from the above date of mailing
International application No.: PCT/US 01/ 31377	International filing date *(day/month/year)*: 04/10/2001

Applicant

CURAGEN CORPORATION

1. This International Searching Authority

(i) considers that there are 6 *(number of)* inventions claimed in the international application covered by the claims indicated ~~below~~/on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~/on the extra sheet:

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(ii) [X] has carried out a partial international search (Rule 40.2) and establishes the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

(1-50) partially

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited,** within the time limit indicated above, to pay the amount indicated below:

EUR 945,00	x	5	=	EUR 4.725,00
Fee per additional invention		number of additional inventions		total amount of additional fees

Or, _____ x _____ = _____

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. [X] Claim(s) Nos. further info _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Henriëtte Huysing-Solles

Form PCT/ISA/206 (July 1992)

INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/US 01/31377

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: (1-50)-partially

An isolated polypeptide comprising an amino acid selected from SEQ ID No. 2; an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide comprising said amino acid sequence; said nucleic acid molecule, wherein said molecule comprisies a nucleic acid sequence SEQ ID No. 1; a vector comprising said nucleic acid molecule; a cell comprising said vector; an antibody that binds immunospecifically to said polypeptide NOV1; a method for determining the presence or amount of said polypepitde in a sample; a method of identifying an agent that binds to said polypeptide; a method for identifying a potential therapeutic agent using said polypeptide; a method for modulating the activity of said polypeptide; a pharmaceutical comprising said polypeptide; a kit comprising said pharmaceutical; a method for screening for a modulator of activity or of latency or predisposition to a pathology associated with said polypeptide; a method for determining the presence of or predisposition to a disease associated with altered levels of said polypepitde;a method of treating a pathological state in a mammal comprising said poylpeptide respectively said antibody;

2. Claims: (1-50)-partially

Idem as invention 1 but limited to NOV2, respectively SEQ ID Nos. 3 and 4.

3. Claims: (1-50)-partially

Idem as invention 1 but limited to NOV3, respectively SEQ ID Nos. 5 and 6;

4. Claims: (1-50)-partially

Idem as invention 1 but limited to NOV4, respectively SEQ ID Nos. 7 and 8.

5. Claims: (1-50)-partially

Idem as invention 1 but limited to NOV5, respectively SEQ ID Nos. 9 and 10.

6. Claims: (1-50)-partially

Idem as invention 1 but limited to NOV6, respectively SEQ ID Nos. 11 and 12.

Motivation of lack of unity

The inventions as defined above relate: (1) to a polypeptide, having internal denomination NOV1, showing homology with UNC5; (2) to a polypeptide, having internal denomination NOV2, showing homology with FAT2; (3) to a polypeptide, having internal denomination NOV3, showing homology with an orphan GPCR; (4) to a polypeptide, having internal denomination NOV4, showing homology with Slit; (5) to a polypeptide, having internal denomination NOV5, showing homology with the AC133 antigen;(6) to a polypeptide, having internal denomination NOV6, showing homology with Spondin 2;

Polypeptides homolog to transmembrane receptor UNC5H1 were already characterized and applications thereof are already known. WO 98/37085 discloses UNC5H1 rat and human sequences and applications of said polypeptides in methods of screening. The polypeptide disclosed in WO 98/37085 as in SEQ ID NO:5 shares 95.991% amino acid sequence identity with the polypeptide of present application as in SEQ ID NO:2, over their entire length.

In view of this prior art, the first problem underlying the present application is the provision of further polypeptides related to UNC5H1. The solution as disclosed and claimed in the present application can be summarised as the provision of a polypeptide comprising an amino acid sequence as in SEQ ID NO:2, related products, methods, compositions and kits.

Further problems are raised and concern the provision of polypeptides related to fat 2 (FAT2) cadherin related tumor suppressor, orphan GPCR, Slit, AC133 antigen, and spondin 2 polypeptide.

The solution is the provision of said proteins, as listed herein above.

Due to the fact UNC5 polypeptides and applications thereof were already known in the prior art, due to the difference in the primary structure of the polypeptides of present invention, due to the essential difference between the problems and the corresponding solutions underlying the application, and due to the fact that no other technical feature can be distinguished which, in the light of the prior art could be regarded as special, common technical feature, the ISA is of the opinion that there is no single inventive concept underlying the plurality of claimed inventions of the present application in the sense of rule 13.2 PCT. Consequentely there is lack of unity and the different inventions, not belonging to a common inventive concept, are formulated as the different subjects on the communication pursuant to Art. 17(3)(a) PCT.

INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/US 01/31377

Form PCT/ISA/206 (extra sheet) (July 1992)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 26-37 and 48-50 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Claims Nos.: 25-partially

Present claim 25 relates to a method involving a compound defined by reference to a desirable characteristic or property, namely its capability to bind to the polypeptide(s) of the invention(s).

The claim covers all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds.
In fact, on page 3, present application states that such a binding compound can be a small molecule, such as a nucleic acid, peptide, polypeptide, peptidomimetic, carbohydrate, lipid or other organic or inorganic molecule.

However, no specific small molecules, nucleic acids, peptides, peptidomimetics, carbohydrates, lipids or other organic or inorganic molecules are disclosed or defined in present application. Moreover, no specific polypeptides, other than antibodies against the polypeptide(s) of present invention(s), are disclosed or defined.

In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claim also lacks clarity (Article 6 PCT). An attempt is made to define a compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

Consequently, the search has been carried out for those parts of the claim which appear to be clear, supported and disclosed, namely those parts relating to a method involving an antibody against the disclosed polypeptide(s).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

PCT/US 01/31377

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:

see 'Invitation to pay additional fees'

2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 01 98354 A (GRIFFIN JENNIFER A;INCYTE GENOMICS INC) 27 December 2001 (2001-12-27) * SEQ ID NO. 1 * the whole document	1-50
E	WO 02 10216 A (ALSOBROOK JOHN P II ;BURGESS CATHERINE (US); GERLACH VALERIE L (US) 7 February 2002 (2002-02-07) * SEQ ID NOS. 1 and 2 * the whole document	1-50
X	WO 98 37085 A (UNIV CALIFORNIA) 27 August 1998 (1998-08-27) * SEQ ID NOS: 1,2,5,6 * the whole document	1-20, 22-26, 28-30, 32-34, 36-44
X	LEONARDO E DAVID ET AL: "Vertebrate homologues of C. elegans UNC-5 are candidate netrin receptors" NATURE, MACMILLAN MAGAZINES, US, vol. 386, no. 6627, 1997, pages 833-838, XP002149239 ISSN: 0028-0836 the whole document	1-20,22, 38-40

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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Form PCT/ISA/206 (Annex, first sheet) (July 1992)

COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No PCT/US 01/31377

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00 73328 A (CRIEKINGE WIM VAN ;DEVGEN NV (BE); BOGAERT THIERRY (BE); ROELENS I) 7 December 2000 (2000-12-07) * SEQ ID NOS: 9,89 * the whole document	1-17
E	WO 01 75440 A (COCHRAN SUSAN ;PATERSON GARY (GB); MORRIS BRIAN (GB); PRATT JUDITH) 11 October 2001 (2001-10-11) * SEQ ID No. 16 * the whole document	1-17
P,X	WO 01 57190 A (CAO YICHENG ;CHEN RUI HONG (US); GOODRICH RYLE (US); HYSEQ INC (US) 9 August 2001 (2001-08-09) * SEQ ID NO. 1790 * the whole document	1-17
P,X	WO 01 53455 A (HYSEQ INC ;LIU CHENGHUA (US); TANG Y TOM (US); DRMANAC RADOJE T (U) 26 July 2001 (2001-07-26) * SEQ ID NO. 1104 * the whole document	1-17

Form PCT/ISA/206 (Annex, continuation sheet)(July 1992)

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